

## An abundant perivascular source of stem cells for bone tissue engineering.

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### Public Summary:

An ideal mesenchymal stem cell (MSC) source for bone tissue engineering has yet to be identified. Such an MSC population would be easily harvested in abundance, with minimal morbidity and with high purity. Our laboratories have identified perivascular stem cells (PSCs) as a candidate cell source. PSCs are readily isolatable (through fluorescent activated cell sorting) from adipose tissue and have been previously shown to be indistinguishable in phenotype and differentiation potential to MSCs. In the present study we describe the reproducible isolation of PSCs from human fat tissue from n = 60 human samples. Patient demographics such as age, gender and body mass index resulted in only a small change in PSC isolation. Next, PSCs were found to have robust bone-forming ability in order to heal surgically created defects in the mouse skull. These data suggest that PSCs are readily and reproducibly obtained from human fat tissue, and have future potential for clinical use in bone regeneration efforts.

### Scientific Abstract:

Adipose tissue is an ideal mesenchymal stem cell (MSC) source, as it is dispensable and accessible with minimal morbidity. However, the stromal vascular fraction (SVF) of adipose tissue is a heterogeneous cell population, which has disadvantages for tissue regeneration. In the present study, we prospectively purified human perivascular stem cells (PSCs) from n = 60 samples of human lipoaspirate and documented their frequency, viability, and variation with patient demographics. PSCs are a fluorescence-activated cell sorting-sorted population composed of pericytes (CD45-, CD146+, CD34-) and adventitial cells (CD45-, CD146-, CD34+), each of which we have previously reported to have properties of MSCs. Here, we found that PSCs make up, on average, 43.2% of SVF from human lipoaspirate (19.5% pericytes and 23.8% adventitial cells). These numbers were minimally changed by age, gender, or body mass index of the patient or by length of refrigerated storage time between liposuction and processing. In a previous publication, we observed that human PSCs (hPSCs) formed significantly more bone in vivo in comparison with unsorted human SVF (hSVF) in an intramuscular implantation model. We now extend this finding to a bone injury model, observing that purified hPSCs led to significantly greater healing of mouse critical-size calvarial defects than hSVF (60.9% healing as opposed to 15.4% healing at 2 weeks postoperative by microcomputed tomography analysis). These studies suggest that adipose-derived hPSCs are a new cell source for future efforts in skeletal regenerative medicine. Moreover, hPSCs are a stem cell-based therapeutic that is readily approvable by the U.S. Food and Drug Administration, with potentially increased safety, purity, identity, potency, and efficacy.

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